

**CONTRAST MEDIA AND ADVERSE REACTIONS
IN INTRAVENOUS UROGRAPHY**

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Introduction

Adverse reactions to intravascularly administered radiological contrast media (CM) may occur immediately on injection or they may be delayed by several hours or days after the examination (Panto and Davies, 1986). The incidences of these reactions during and after intravenous urography (IVU) were investigated at St Luke's Hospital.

Methodology

Two surveys were carried out over an 11-week period. In the first survey, 321 patients (199 males; 122 females) were interviewed to determine the presence or absence of a history of exposure to CM, of allergy and of underlying conditions and diseases. The patients were then monitored during and after the injection of an ionic CM (Urografin^R 60% w/v, Schering AG) to determine the time of onset, signs and symptoms and severity of immediate adverse reactions, and the treatment given.

Data for the second survey on delayed adverse reactions were collected by means of a questionnaire distributed to 121 patients (42 males; 39 females) amongst the participants in Survey 1. The questions enquired on the presence, the time of onset and the duration of arm pain and rashes, and the presence of any other signs and symptoms. The questionnaires were to be returned one week after the IVU examination.

A study was also performed to determine the costs that would be involved in a changeover from ionic CM to nonionic CM in IVU. The information on prices and number of patients examined by IVU was obtained from the Government Medical Stores and the Department of Radiology respectively.

Results

Survey 1

1. Incidence of adverse reactions: 35.2% (n=113) experienced a reaction that was mild (32.4%, n=104) or moderate (2.8%, n=9) in severity. The signs and symptoms which occurred include: heat sensation (n=79), nausea (n=40), vomiting (n=11), retching (n=8), erythema (n=3), sneezing (n=3), urticaria (n=2), itching (n=1), arm pain (n=1), coughing (n=1), chest pain (n=1), dizziness (n=1), choking sensation (n=1), and

nasal congestion (n=1). 82.3% (n=93) of the reactions took place during the injection of the CM.

2. Incidence by patient age: The age of the patients ranged from 10-101 years (mean age = 49.3 years). The highest incidence was in patients aged 40-49 years (47.6%) and the lowest incidence was in the 70-79 year age group (16.7%).
3. Incidence by history of previous reactions: Reactions occurred in 81.8% of patients with a history of reactions and in 24.6% of patients with a history of exposure to a CM but not of reactions.
4. Incidence by history of allergy and underlying conditions: 40% of patients with a history of allergy (asthma, hay fever, urticaria, food and/or drugs) and 34.5% of patients with no allergies experienced an adverse reaction. The highest incidences of reactions were reported for thyroid disorders (80%), anxiety (63.2%), blood dyscrasias (50%), respiratory diseases (40%) and renal disease (38.9%).
5. Incidence by dose of CM: A dose of 1 ml/kg body weight provided the lowest incidence of reactions possible (33.3%) at an optimum radiodensity.
6. Effect of pretreatment: Heat sensation was reported by 2 patients out of 6 who were pretreated with an antihistamine or a corticosteroid immediately prior to the injection of the CM.
7. Treatment of adverse reactions: One or more drugs (clemastine, clemizole, metoclopramide, hydrocortisone and/or dexamethasone) were administered to 14 patients with a mild reaction and to 9 patients with a moderate reaction for the prophylaxis or symptomatic treatment of reactions.

Survey 2

66.9% (n=81) of the patients returned the questionnaire.

1. Incidence of delayed adverse reactions: 48.1% (n=39) of patients reported a delayed reaction. 19.8% (n=16) had arm pain and 18.5% (n=15) had a rash. 42.9% of the symptoms reported as free text comments were indicative of iodine toxicity (tiredness, constipation, abdominal pain, headache).

2. Onset and duration of delayed reactions: The time of onset of arm pain ranged from 0-3 days after IVU and lasted for 12 hours to 7 days. Rashes appeared within 5 hours to 3 days and lasted for 20 minutes to 2 days.
3. Relationship between immediate and delayed adverse reactions: 51.4% of patients with an immediate reaction and 45.7% of patients without an immediate reaction experienced a delayed reaction.
4. Skin reactions: A delayed skin reaction occurred in 31.8% of patients with a history of allergy and in 13.8% with a negative history and in 17.5% of patients without an immediate skin reaction. Delayed reactions were more frequent (18.5%, n=15) than immediate reactions (1.2%, n=1).

Cost of ionic and nonionic CM

Table 1 demonstrates that nonionic CM is 12-17 times more expensive than ionic CM.

Table 1: Cost of ionic and nonionic contrast media at St Luke's Hospital

Contrast Medium	Volume of Ampoule	Hospital Price (per gram of iodine)
Ionic: Diatrizoate (Urografin 60% w/v, Schering AG)	20 ml	Lm0.06,3
Nonionic: Iohexol (Omnipaque 300 mg I/ml, Nycomed AS)	10ml 50ml	Lm1.08,3 Lm0.80,6

The cost of CM for an average of 2605 IVU examinations per year and an average dose of 63.9 ml per patient was estimated to be LM3,054/year if diatrizoate only is administered and Lm43,244/year if iohexol only is administered. The cost of prophylactic or symptomatic treatment of adverse reactions in 27 patients out of 321 in Survey 1 was Lm3,93,6.

Assuming that the same proportion of patients is treated in a year, then the annual cost of the drug therapy would be Lm31.92,5.

Discussion

Table 2 demonstrates that the incidence of immediate adverse reactions to ionic CM in IVU in Malta is high. However, in the studies by Shehadi and Toniolo (1980) and Palmer (1988), the sensation of heat was not recorded as an adverse reaction. Palmer further stated that mild reactions were underreported and nausea and other mild symptoms were frequently ignored as mild reactions. Ansell (1987) also noted underreporting and inconsistent reporting of adverse reactions. If heat sensation were excluded from the Maltese Study, the incidence of adverse reactions would be 15.9%.

Table 2: A comparison of surveys on adverse reactions to ionic contrast media

Study	Country of Origin	% Incidence of Adverse Reactions
Malta (1991) [#]	Malta	35.2%
Shehadi & Toniolo (1980) [#]	N.America, Europe, Australia	4.8%
Ansell (1987) [#]	United Kingdom	8.3%
Palmer (1988) ^{\$}	Australia	3.8%
Katamaya et al (1990) ^{\$}	Japan	12.7%

Note: # surveys on intravenous urography only
 \$ surveys on all intravascular contrast examinations

The incidence of delayed adverse reactions to ionic and nonionic urographic CM was 30% in a U.K. study (Panto and Davies, 1986). This is lower than the 48.1% incidence in Malta but 29% of the U.K. participants

were administered a nonionic CM whereas Maltese patients received only an ionic CM.

Adverse reactions are reduced by a factor of 3-4 when nonionic CM are administered instead of ionic CM (Palmer, 1988; Katamaya et al, 1990). However, the universal use of nonionic CM would place a financial burden on the State Pharmaceutical Services since the expenditure would be 14 times greater than with ionic CM only.

Conclusion

The monitoring of patients for immediate and delayed adverse reactions is essential in IVU. Drugs and equipment for resuscitation should be readily available for the prompt treatment of severe reactions. A clinical pharmacist can play a role in providing an information and monitoring service for delayed reactions. It is being proposed that a record of CM administered to patients should be kept to provide the necessary data for the management of delayed reactions and for epidemiological purposes. A recommendation is being made for the drawing up of a protocol on the use of nonionic CM in high risk patients and the pretreatment of patients receiving ionic CM to lower the incidence of adverse reactions.

References

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